Sequence information

Length: **258 AA** [This is the length of the unprocessed precursor]	Molecular weight: **29335 Da** [This is the MW of the unprocessed precursor]	CRC64: **0F7EBAE62069A5D0** [This is a checksum on the sequence]

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         10         20         30         40         50         60
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MVKIIFVFFI FLSSFSYAND DKLYRADSRP PDEIKQSGGL MPRGQSEYFD RGTQMNINLY

         70         80         90        100        110        120
          |          |          |          |          |          |
DHARGTQTGF VRHDDGYVST SISLRSAHLV GQTILSGHST YYIYVIATAP NMFNVNDVLG

        130        140        150        160        170        180
          |          |          |          |          |          |
AYSPHPDEQE VSALGGIPYS QIYGWYRVHF GVLDEQLHRN RGYRDRYYSN LDIAPAADGY

        190        200        210        220        230        240
          |          |          |          |          |          |
GLAGFPPEHR AWREEPWIHH APPGCGNAPR SSMSNTCDEK TQSLGVKFLD EYQSKVKRQI

        250
          |
FSGYQSDIDT HNRIKDEL
```

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ScanProsite, MotifScan

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The Korean ExPASy site, **kr.expasy.org**, is temporarily not available.

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[General] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

General information about the entry

Entry name	**CHTA_VIBCH**
Primary accession number	**P01555**
Secondary accession numbers	Q56634 Q9JPV1
Entered in Swiss-Prot in	Release 01, July 1986
Sequence was last modified in	Release 02, October 1986
Annotations were last modified in	Release 41, February 2003
Name and origin of the protein	
Protein name	**Cholera enterotoxin, A chain [Precursor]**
Synonyms	**NAD(+)--diphthamide ADP-ribosyltransferase** **EC 2.4.2.36** **Cholera enterotoxin A subunit**
Gene name	**CTXA** or **TOXA** or **VC1457**
From	Vibrio cholerae [TaxID: 666]
Taxonomy	Bacteria; Proteobacteria; Gammaproteobacteria; Vibrionales; Vibrionaceae; Vibrio.

References

[1]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=El Tor 2125; MEDLINE=84068199; PubMed=6646234; [NCBI, ExPASy, EBI, Israel, Japan] Mekalanos J.J., Swartz D.J., Pearson G.D.N., Harford N., Groyne F., de Wilde M.; "Cholera toxin genes: nucleotide sequence, deletion analysis and vaccine development."; Nature 306:551-557(1983).
[2]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=Classical 569B / ATCC 25870 / Serotype O1; MEDLINE=91355224; PubMed=1883840; [NCBI, ExPASy, EBI, Israel, Japan] Dams E., de Wolf M., Dierick W.; "Nucleotide sequence analysis of the CT operon of the Vibrio cholerae

	classical strain 569B."; Biochim. Biophys. Acta 1090:139-141(1991).
[3]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=1854 / O139-Bengal; Yamamoto K., Do V.G.R.F., Xu M., Iida T., Miwatani T., Albert M.J., Honda T.; Submitted (MAY-1994) to the EMBL/GenBank/DDBJ databases.
[4]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=El Tor 2125; Dams E., de Wolf M., Dierick W.; Submitted (MAY-1991) to the EMBL/GenBank/DDBJ databases.
[5]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=KNIH002; Shin H.J., Park Y.C., Kim Y.C.; "Cloning and nucleotide sequence analysis of the virulence gene cassette from Vibrio cholerae KNIH002 isolated in Korea."; Misainmurhag Hoiji 35:205-210(1999).
[6]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=El Tor N16961 / Serotype O1; MEDLINE=20406833; PubMed=10952301; [NCBI, ExPASy, EBI, Israel, Japan] Heidelberg J.F., Eisen J.A., Nelson W.C., Clayton R.A., Gwinn M.L., Dodson R.J., Haft D.H., Hickey E.K., Peterson J.D., Umayam L.A., Gill S.R., Nelson K.E., Read T.D., Tettelin H., Richardson D., Ermolaeva M.D., Vamathevan J., Bass S., Qin H., Dragoi I., Sellers P., McDonald L., Utterback T., Fleischmann R.D., Nierman W.C., White O., Salzberg S.L., Smith H.O., Colwell R.R., Mekalanos J.J., Venter J.C., Fraser C.M.; "DNA sequence of both chromosomes of the cholera pathogen Vibrio cholerae."; Nature 406:477-483(2000).
[7]	SEQUENCE OF 1-212 FROM NUCLEIC ACID. **STRAIN**=Classical 569B / ATCC 25870 / Serotype O1; MEDLINE=85006737; PubMed=6090390; [NCBI, ExPASy, EBI, Israel, Japan] Lockman H.A., Galen J.E., Kaper J.B.;

	"Vibrio cholerae enterotoxin genes: nucleotide sequence analysis of DNA encoding ADP-ribosyltransferase."; J. Bacteriol. 159:1086-1089(1984).
[8]	SEQUENCE OF 213-258 FROM NUCLEIC ACID. MEDLINE=84061784; PubMed=6315707; [NCBI, ExPASy, EBI, Israel, Japan] Lockman H., Kaper J.B.; "Nucleotide sequence analysis of the A2 and B subunits of Vibrio cholerae enterotoxin."; J. Biol. Chem. 258:13722-13726(1983).
[9]	SEQUENCE OF 19-27. MEDLINE=81212799; PubMed=7238869; [NCBI, ExPASy, EBI, Israel, Japan] Duffy L.K., Peterson J.W., Kurosky A.; "Isolation and characterization of a precursor form of the 'A' subunit of cholera toxin."; FEBS Lett. 126:187-190(1981).
[10]	SEQUENCE OF 19-38 AND 213-232. MEDLINE=76259136; PubMed=955672; [NCBI, ExPASy, EBI, Israel, Japan] Klapper D.G., Finkelstein R.A., Capra J.D.; "Subunit structure and N-terminal amino acid sequence of the three chains of cholera enterotoxin."; Immunochemistry 13:605-611(1976).
[11]	SEQUENCE OF 27-72 AND 111-139. MEDLINE=79169830; PubMed=437113; [NCBI, ExPASy, EBI, Israel, Japan] Lai C.-Y., Cancedda F., Chang D.; "Primary structure of cholera toxin subunit A1: isolation, partial sequences and alignment of the BrCN fragments."; FEBS Lett. 100:85-89(1979).
[12]	SEQUENCE OF 213-258. MEDLINE=82053094; PubMed=7028752; [NCBI, ExPASy, EBI, Israel, Japan] Duffy L.K., Peterson J.W., Kurosky A.;

	"Covalent structure of the gamma chain of the A subunit of cholera toxin."; J. Biol. Chem. 256:12252-12256(1981).
[13]	X-RAY CRYSTALLOGRAPHY (2.4 ANGSTROMS). MEDLINE=95387395; PubMed=7658473; [NCBI, ExPASy, EBI, Israel, Japan] Zhang R.G., Scott D.L., Westbrook M.L., Nance S., Spangler B.D., Shipley G.G., Westbrook E.M.; "The three-dimensional crystal structure of cholera toxin."; J. Mol. Biol. 251:563-573(1995).

Comments

FUNCTION: THE ALPHA/GAMMA CHAIN (A SUBUNIT) IS AN ADP-RIBOSYLATING TOXIN.

CATALYTIC ACTIVITY: NAD^+ + peptide diphthamide = nicotinamide + peptide N-(ADP-D-ribosyl)diphthamide.

SUBUNIT: CONTAINS 3 KINDS OF CHAINS. AN ALPHA AND A GAMMA CHAIN (FROM THE SAME PRECURSOR MOLECULE), LINKED BY AN INTERCHAIN DISULFIDE BOND, ASSOCIATE NONCOVALENTLY WITH AN AGGREGATE OF 4 TO 6 BETA CHAINS.

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Cross-references

EMBL	X00171; CAA24995.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] X58785; CAA41590.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] D30053; BAA06290.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] X58786; CAA41592.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] K02679; AAA27514.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] AF175708; AAD51359.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] AE004224; AAF94614.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] K01170; AAA27572.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] D30052; BAA06288.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	A05129; XVVCA.
PDB	1XPB; 01-APR-97. [ExPASy / RCSB] 1XTC; 01-AUG-96. [ExPASy / RCSB] Detailed list of linked structures.
TIGR	VC1457; -.
InterPro	IPR001144; Enterotoxin_A. Graphical view of domain structure.
Pfam	PF01375; Enterotoxin_A; 1.
PRINTS	PR00771; ENTEROTOXINA.
ProDom	[Domain structure / List of seq. sharing at least 1 domain]
HOBACGEN	[Family / Alignment / Tree]
BLOCKS	P01555.
ProtoNet	P01555.
ProtoMap	P01555.
PRESAGE	P01555.

DIP	P01555.
ModBase	P01555.
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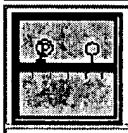
Keywords

Enterotoxin; Signal; NAD; Transferase; Glycosyltransferase; 3D-structure; Complete proteome.

Features

 Feature table viewer

 Feature aligner

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SIGNAL	1	18	18	
CHAIN	19	212	194	CHOLERA ENTEROTOXIN, CHAIN-A1 (ALPHA).
CHAIN	213	258	46	CHOLERA ENTEROTOXIN, CHAIN-A2 (GAMMA).
DISULFID	217	217		INTERCHAIN (WITH GAMMA CHAIN).
ACT_SITE	62	62		INTERACT WITH NAD (*BY SIMILARITY*).
ACT_SITE	130	130		*BY SIMILARITY*.
CONFLICT	20	20		D -> N (IN REF. 9).
CONFLICT	37	37		S -> R (IN REF. 10).
CONFLICT	39	39		G -> L (IN REF. 11).
CONFLICT	45	46		QS -> SE (IN REF. 11).
CONFLICT	111	111		N -> L (IN REF. 11).
CONFLICT	132	132		S -> A (IN REF. 11).
CONFLICT	213	213		M -> I (IN REF. 1).
CONFLICT	247	248		DI -> ID (IN REF. 12).
CONFLICT	256	256		D -> N (IN REF. 12).
STRAND	24	27	4	
HELIX	31	37	7	
TURN	38	38	1	
STRAND	39	40	2	
TURN	43	44	2	
TURN	48	49	2	

9 differences

HELIX	59	63	5
TURN	64	64	1
TURN	75	76	2
STRAND	77	81	5
HELIX	85	89	5
TURN	90	91	2
TURN	96	97	2
STRAND	101	106	6
TURN	110	111	2
STRAND	112	114	3
HELIX	115	119	5
HELIX	120	122	3
HELIX	126	128	3
STRAND	130	134	5
STRAND	137	138	2
TURN	139	141	3
STRAND	142	148	7
STRAND	153	159	7
TURN	161	162	2
HELIX	165	168	4
TURN	169	170	2
HELIX	176	178	3
TURN	187	188	2
HELIX	190	193	4
TURN	195	196	2
HELIX	197	199	3
TURN	200	200	1
TURN	203	204	2
HELIX	215	251	37
TURN	252	253	2
HELIX	254	258	5

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MVKIIFVFFI FLSSFSYAND DKLYRADSRP PDEIKQSGGL MPRGQSEYFD RGTQMNINLY

        70          80          90         100         110         120
         |           |           |           |           |           |
DHARGTQTGF VRHDDGYVST SISLRSAHLV GQTILSGHST YYIYVIATAP NMFNVNDVLG

       130         140         150         160         170         180
         |           |           |           |           |           |
AYSPHPDEQE VSALGGIPYS QIYGWYRVHF GVLDEQLHRN RGYRDRYYSN LDIAPAADGY

       190         200         210         220         230         240
         |           |           |           |           |           |
GLAGFPPEHR AWREEPWIHH APPGCGNAPR SSMSNTCDEK TQSLGVKFLD EYQSKVKRQI

       250
         |
FSGYQSDIDT HNRIEDEL
```

Q8L356 in FASTA format

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General information about the entry

Entry name	**Q8L356**
Primary accession number	**Q8L356**
Secondary accession numbers	None
Entered in TrEMBL in	Release 22, October 2002
Sequence was last modified in	Release 22, October 2002
Annotations were last modified in	Release 24, June 2003

Name and origin of the protein

Protein name	**Cholera toxin A subunit**
Synonyms	None
Gene name	**CTXA**
From	Vibrio cholerae O27 [TaxID: 185331]
Taxonomy	Bacteria; Proteobacteria; Gammaproteobacteria; Vibrionales; Vibrionaceae; Vibrio.

References

[1] SEQUENCE FROM NUCLEIC ACID.
STRAIN=365-96;
MEDLINE=21950561; PubMed=11953381; [NCBI, ExPASy, EBI, Israel, Japan]
Li M., Shimada T., Morris J.G. Jr., Sulakvelidze A., Sozhamannan S.;
"Evidence for the emergence of non-O1 and non-O139 Vibrio cholerae strains with pathogenic potential by exchange of O-antigen biosynthesis regions.";
Infect. Immun. 70:2441-2453(2002).

Comments

None

Cross-references

EMBL	AF390572; AAM22586.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
GO	GO:0005576; Cellular component: extracellular *(inferred from electronic annotation).* GO:0015070; Molecular function: toxin activity *(inferred from electronic annotation).* GO:0009405; Biological process: pathogenesis *(inferred from electronic annotation).*
InterPro	IPR001144; Enterotoxin_A. Graphical view of domain structure.
Pfam	PF01375; Enterotoxin_A; 1.
PRINTS	PR00771; ENTEROTOXINA.
ProDom	[Domain structure / List of seq. sharing at least 1 domain]
HOBACGEN	[Family / Alignment / Tree]
ProtoMap	Q8L356.
PRESAGE	Q8L356.
ModBase	Q8L356.
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Keywords

None

Features

None

Sequence information

Length: **258 AA**	Molecular weight: **29336 Da**	CRC64: **0F7EBAEE0069A5D0** [This is a checksum on the sequence]

Length: **258 AA**	Molecular weight: **29362 Da**	CRC64: **3EA358C7F8BA8BF7** [This is a checksum on the sequence]

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MVKIIFVFFI FLSSFSYAND DKLYRADSRP PDEIKQSGGL MPRGQNEYFD RGTQMNINLY

        70         80         90        100        110        120
         |          |          |          |          |          |
DHARGTQTGF VRHDDGYVST SISLRSAHLV GQTILSGHST YYIYVIATAP NMFNVNDVLG

       130        140        150        160        170        180
         |          |          |          |          |          |
AYSPHPDEQE VSALGGIPYS QIYGWYRVHF GVLDEQLHRN RGYRDRYYSN LDIAPAADGY

       190        200        210        220        230        240
         |          |          |          |          |          |
GLAGFPPEHR AWREEPWIHH APPGCGNAPR SSMSNTCDEK TQSLGVKFLD EYQSKVKRQI

       250
         |
FSGYQSDIDT HNRIKDEL
```

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[General] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

General information about the entry

Entry name	**Q8VLI6**
Primary accession number	**Q8VLI6**
Secondary accession numbers	None
Entered in TrEMBL in	Release 20, March 2002
Sequence was last modified in	Release 20, March 2002
Annotations were last modified in	Release 24, June 2003

Name and origin of the protein

Protein name	***CtxA***
Synonyms	None
Gene name	***CTXA***
From	Vibrio cholerae [TaxID: 666]
Taxonomy	Bacteria; Proteobacteria; Gammaproteobacteria; Vibrionales; Vibrionaceae; Vibrio.

References

[1]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=203-93, and 571-88; Li M., Chen Y., Kotetishvili M., Stine O.C., Morris J.G. Jr., Sulakvelidze A., Sozhamannan S.; "Genetic Analysis of the Virulence Regions, CTX f prophage and Vibrio Pathogenicity Island (VPI), in Diverse, Non-epidemic Serogroup Strains of Vibrio cholerae."; Submitted (DEC-2001) to the EMBL/GenBank/DDBJ databases.
[2]	SEQUENCE FROM NUCLEIC ACID. **STRAIN**=1322-69; Li M., Chen Y., Kotetishvili M., Stine O.C., Morris J.G. Jr., Sulakvelidze A., Sozhamannan S.; "Genetic Analysis of the Virulence Regions, CTX f prophage and Vibrio Pathogenicity Island (VPI), in Diverse, Non-epidemic Serogroup Strains of Vibrio cholerae."; Submitted (NOV-2001) to the EMBL/GenBank/DDBJ databases.

Comments

None

Cross-references

EMBL	AF463401; [EMBL / GenBank / DDBJ] AAL69945.1; -. [CoDingSequence] AF452584; [EMBL / GenBank / DDBJ] AAL60525.1; -. [CoDingSequence] AF463400; [EMBL / GenBank / DDBJ] AAL69944.1; -. [CoDingSequence]
GO	GO:0005576; Cellular component: extracellular *(inferred from electronic annotation).* GO:0015070; Molecular function: toxin activity *(inferred from electronic annotation).* GO:0009405; Biological process: pathogenesis *(inferred from electronic annotation).*
InterPro	IPR001144; Enterotoxin_A. IPR000886; ER_target. Graphical view of domain structure.
Pfam	PF01375; Enterotoxin_A; 1.
PRINTS	PR00771; ENTEROTOXINA.
PROSITE	PS00014; ER_TARGET; 1.
ProDom	[Domain structure / List of seq. sharing at least 1 domain]
HOBACGEN	[Family / Alignment / Tree]
ProtoMap	Q8VLI6.
PRESAGE	Q8VLI6.
ModBase	Q8VLI6.
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Keywords

None

Features

None

Sequence information

WEST Search History

109

DATE: Thursday, June 26, 2003

Set Name side by side	Query	Hit Count	Set Name result set
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L3	L1 and meningitidis.clm.	1	L3
L4	L1 and (gd-2 or gd2).clm.	3	L4
L5	L1 and (rota$ and syncytial).clm.	9	L5
L6	helicobacter.clm. and pylori.clm. urease.clm. and vaccin$.clm.	6	L6
L7	pora.clm.	1	L7
L8	haemophilus.clm. and p4.clm. and p6.clm.	0	L8
L9	haemophilus.clm. and p4.clm.	0	L9
L10	p4.clm. and p6.clm. and hap$.clm.	0	L10
L11	p4.clm. and p6.clm.	83	L11
L12	L11 and influenz$.clm.	0	L12
L13	influenz$.clm.	1067	L13
L14	L13 and (opp$ and adher$).clm.	1	L14
L15	L13 and (omp$ and adher$).clm.	0	L15
L16	L13 and (omp$).clm.	5	L16
L17	L13 and (omp near10 p4)	4	L17
L18	L13 and (hap or haps! or hap-s!)	11	L18
L19	('6245337')[PN]	1	L19

END OF SEARCH HISTORY

WEST

Search Results - Record(s) 1 through 1 of 1 returned.

L19: Entry 1 of 1 File: USPT Jun 12, 2001

US-PAT-NO: 6245337
DOCUMENT-IDENTIFIER: US 6245337 B1

TITLE: Haemophilus adherence and penetration proteins

DATE-ISSUED: June 12, 2001

US-CL-CURRENT: 424/256.1; 424/190.1, 435/69.1, 435/69.3, 530/350

INT-CL: [07] A61 K 39/102

Previous Page Next Page

WEST Search History

DATE: Thursday, June 26, 2003

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L2	(e29 or e-29 or glu29 or glu-29) same (cholera or ctx or rctx or cta or adpribosy$ or ribosylat$ or adp-ribosyla$ or mucosal)	0	L2
L3	(e29 or e-29 or glu29 or glu-29).clm. and (cholera or ctx or rctx or cta or adpribosy$ or ribosylat$ or adp-ribosyla$ or mucosal).clm.	0	L3
L4	(e29 or e-29 or glu29 or glu-29).clm.	6	L4
L5	(e29 or e-29 or glu29 or glu-29) and cholera	2	L5
L6	(e29 or e-29 or glu29 or glu-29) and (adpribosy$ or adp)	10	L6

END OF SEARCH HISTORY

08955989 20245740 PMID: 10781860

Effective mucosal immunization against respiratory syncytial virus using purified F protein and a genetically detoxified cholera holotoxin, CT- E29H

Tebbey P W; Scheuer C A; Peek J A; Zhu D; LaPierre N A; Green B A; Phillips E D; Ibraghimov A R; Eldridge J H; Hancock G E

Department of Immunology Research, Wyeth-Lederle Vaccines, 211 Bailey Road, West Henrietta, NY 14586-9728, USA.

Vaccine (ENGLAND) Jun 1 2000, 18 (24) p2723-34, ISSN 0264-410X Journal Code: 8406899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

We exploited the powerful adjuvant properties of cholera holotoxin (CT) to create a mucosally administered subunit vaccine against respiratory syncytial virus (RSV). A genetically detoxified mutant CT with an E to H substitution at amino acid 29 of the CT-A1 subunit (CT- **E29H**) was compared to wild type CT for toxicity and potential use as an intranasal (IN) adjuvant for the natural fusion (F) protein of RSV. When compared to CT the results demonstrated that: (1) CT- **E29H** binding to GM1 ganglioside was equivalent, (2) ADP-ribosylation of agmatine was 11.7%, and (3) toxicity was attenuated in both Y-1 adrenal (1.2%) and patent mouse gut weight assays. IN vaccination with F protein formulated with CT- **E29H** induced serum anti-CT and anti-F protein antibodies that were comparable to those obtained after vaccination with equivalent doses of CT. Vaccinations containing CT- **E29H** at doses of 0.1 microg were statistically equivalent to 1.0 microg in enhancing responses to F protein. Antigen-specific mucosal IgA and anti-RSV neutralizing antibodies were detected in nasal washes and sera, respectively, of mice that had received F protein and 0.1 or 1.0 microg of CT- **E29H** . Anti-F protein IgA was not detected in the nasal washes from mice IN vaccinated with 0.01 microg CT- **E29H** or IM with F protein adsorbed to AlOH adjuvant. In addition, the formulation of purified F protein and CT- **E29H** (0.1 and 1.0 microg) facilitated protection of both mouse lung and nose from live RSV challenge. Collectively, the data have important implications for vaccine strategies that use genetically detoxified mutant cholera holotoxins for the mucosal delivery of highly purified RSV antigens.

Tags: Animal; Female

Descriptors: *Antigens, Viral--immunology--IM; *Cholera Toxin--immunology--IM; *Respiratory Syncytial Viruses--immunology--IM; *Viral Proteins--immunology--IM; *Viral Vaccines--immunology--IM; Bronchoalveolar Lavage; Electrophoresis, Polyacrylamide Gel; Enzyme-Linked Immunosorbent Assay; Immunity, Mucosal; Lung--virology--VI; Mice; Mice, Inbred BALB C; Nasal Mucosa--virology--VI

CAS Registry No.: 0 (Antigens, Viral); 0 (Viral Proteins); 0 (Viral Vaccines); 0 (attachment protein G); 0 (respiratory syncytial virus proteins); 9012-63-9 (Cholera Toxin)

Record Date Created: 20000711

Record Date Completed: 20000711

09403284 21169659 PMID: 11270595

Protective efficacy of rotavirus 2/6-virus-like particles combined with CT- E29H , a detoxified cholera toxin adjuvant.

Siadat-Pajouh M; Cai L

Department of Viral Vaccine Research, Wyeth-Lederle Vaccines, Pearl River, New York, USA.

Viral immunology (United States) 2001, 14 (1) p31-47, ISSN 0882-8245 Journal Code: 8801552

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Identifying a safe and efficacious mucosal adjuvant is crucial for the development of subunit vaccines against rotavirus and other mucosal pathogens. Moreover, recognition of determinants of protective immunity to rotavirus infection is essential to the design of the means to prevent or control this viral gastrointestinal disease. We have studied the kinetics of systemic and mucosal antibody responses elicited upon mucosal immunization of mice with rotavirus recombinant virus-like particles (rVLPs) alone or combined with a detoxified version of cholera toxin, CT- **E29H** . CT- **E29H** has been shown to maintain the adjuvant effect of parental cholera holotoxin. Both inbred BALB/c and outbred CD-1 mice were immunized with rotavirus VP2/6-rVLPs (2/6-VLPs) combined with CT- **E29H** , orally or intranasally (i.n.), and the comparative efficacy of different formulations was then determined. Rotavirus-specific serum and fecal IgA, IgM, and IgG antibodies were determined by enzyme-linked immunoadsorbent assay (ELISA) weekly (or every other week) following vaccination. Animals then were challenged with a murine rotavirus strain, EDIM. The degree to which vaccinated animals were protected from the wild-type rotavirus challenge was reflected in the levels of viral antigen shed in stools (percent reduction in antigen shedding, PRAS). BALB/c mice immunized by either route produced rotavirus-specific serum IgA, IgM and IgG, as well as fecal IgA and IgG, but not IgM; however, the intranasal immunization induced stronger systemic IgG and IgM responses than did oral immunization. Similar levels of prechallenge rotavirus-specific fecal and serum IgA were detected in both the orally and the i.n. immunized groups. Two immunizations with 2-6VLPs and CT- **E29H** were sufficient to protect BALB/c mice, regardless of the route of administration. PRAS was 99.6, 98.8, and 98.8% for oral, i.n. and the oral + i.n. groups, respectively; in contrast vaccination with 2/6-VLPs alone was not protective (PRAS = 39%), indicating the critical role of CT- **E29H** in inducing protective levels of immune responses. Two of four outbred CD-1 mice that were immunized orally with 2/6-VLPs-CT- **E29H** showed no humoral responses (PRAS, 65%), but four of four i.n. immunized CD-1 mice displayed humoral responses (PRAS, 97.9%). Serum anti-VP6 and VP2 antibodies were detected in all immunoresponsive mice. The combined results in two strains of mice indicate that CTE29H is an effective mucosal adjuvant capable of inducing protective immune responses and suggest that intranasal administration is the preferred route of immunization.

Tags: Animal; Human

Descriptors: *Capsid--immunology--IM; *Cholera Toxin--immunology--IM; *Rotavirus Infections--prevention and control--PC; *Rotavirus Vaccines --immunology--IM; Adjuvants, Immunologic; Antibodies, Viral--blood--BL; Capsid--genetics--GE; Capsid Proteins; Disease Models, Animal; Feces --chemistry--CH; Immunization; Immunoglobulin A, Secretory--analysis--AN; Mice; Mice, Inbred BALB C; Recombinant Proteins--immunology--IM; Rotavirus --immunology--IM; Rotavirus Infections--immunology--IM; Rotavirus Vaccines --administration and dosage--AD; Virion--genetics--GE; Virion--immunology --IM

09472592 21246685 PMID: 11349048

Recombinant PhpA protein, a unique histidine motif-containing protein from Streptococcus pneumoniae, protects mice against intranasal pneumococcal challenge.

Zhang Y; Masi A W; Barniak V; Mountzouros K; Hostetter M K; Green B A

Department of Immunology, Wyeth Lederle Vaccines, West Henrietta, New York 14586-9728, USA. zhangy4@war.wyeth.com

Infection and immunity (United States) Jun 2001, 69 (6) p3827-36, ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI 24162; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The multivalent pneumococcal conjugate vaccine is effective against both systemic disease and otitis media caused by serotypes contained in the vaccine. However, serotypes not covered by the current conjugate vaccine may still cause pneumococcal disease. To address these serotypes and the remaining otitis media due to Streptococcus pneumoniae, we have been evaluating antigenically conserved proteins from S. pneumoniae as vaccine candidates. A previous report identified a 20-kDa protein with putative human complement C3-proteolytic activity. By utilizing the publicly released pneumococcal genomic sequences, we found the gene encoding the 20-kDa protein to be part of a putative open reading frame of approximately 2,400 bp. We recombinantly expressed a 79-kDa fragment (rPhpA-79) that contains a repeated HxxHxH motif and evaluated it for vaccine potential. The antibodies elicited by the purified rPhpA-79 protein were cross-reactive to proteins from multiple strains of S. pneumoniae and were against surface-exposed epitopes. Immunization with rPhpA-79 protein adjuvanted with monophosphoryl lipid A (for subcutaneous immunization) or a mutant cholera toxin, CT- **E29H** (for intranasal immunization), protected CBA/N mice against death and bacteremia, as well as reduced nasopharyngeal colonization, following intranasal challenge with a heterologous pneumococcal strain. In contrast, immunization with the 20-kDa portion of the PhpA protein did not protect mice. These results suggest that rPhpA-79 is a potential candidate for use as a vaccine against pneumococcal systemic disease and otitis media.

Tags: Animal; Human; Male; Support, U.S. Gov't, P.H.S.

Descriptors: *Bacterial Proteins--genetics--GE; *Endopeptidases --immunology--IM; *Otitis Media--prevention and control--PC; *Pneumococcal Infections--prevention and control--PC; *Streptococcal Vaccines--immunology --IM; *Streptococcus pneumoniae--immunology--IM; Administration, Intranasal ; Antibodies, Bacterial--blood--BL; Bacterial Proteins--immunology--IM; Endopeptidases--chemistry--CH; Endopeptidases--genetics--GE; Endopeptidas es--metabolism--ME; Histidine--chemistry--CH; Immunization; Mice; Mice, Inbred CBA; Molecular Sequence Data; Nasopharynx--microbiology--MI; Otitis Media--microbiology--MI; Pneumococcal Infections--microbiology--MI; Recombinant Proteins--genetics--GE; Recombinant Proteins--immunology--IM; Recombinant Proteins--metabolism--ME; Sequence Analysis, DNA

Molecular Sequence Databank No.: GENBANK/AF340221; GENBANK/AF340222; GENBANK/AF340223

CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Bacterial Proteins); 0 (PhpA protein); 0 (Recombinant Proteins); 0 (Streptococcal Vaccines) ; 71-00-1 (Histidine)

Enzyme No.: EC 3.4.- (Endopeptidases)

Record Date Created: 20010511

Record Date Completed: 20010628

13971796 22242173 PMID: 12355362

Immunization with Haemophilus influenzae Hap adhesin protects against nasopharyngeal colonization in experimental mice.

Cutter David; Mason Kathryn W; Howell Alan P; Fink Doran L; Green Bruce A ; St Geme Joseph W; et al

Edward Mallinckrodt Department of Pediatrics, Washington University School of Medicine, 660 S. Euclid Avenue, St. Louis, MO 63110, USA.

Journal of infectious diseases (United States) Oct 15 2002, 186 (8) p1115-21, ISSN 0022-1899 Journal Code: 0413675

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Nontypeable Haemophilus influenzae is a common cause of respiratory tract disease and initiates infection by colonizing the nasopharynx. The H. influenzae Hap adhesin is an autotransporter protein that was discovered because it promotes intimate interaction with human epithelial cells. Hap contains an extracellular domain called Hap(s) that has adhesive and protease activity and an outer membrane domain called Hap(beta) that serves to present Hap(s) on the surface of the cell. Hap(s) purified from nontypeable H. influenzae strain P860295 was used to immunize BALB/c mice intranasally. Immunization stimulated significant mucosal and serum anti-Hap(s) antibody titers, which were augmented by the addition of mutant cholera toxin (CT- **E29H**) as an adjuvant. Immunization was associated with a marked reduction in the density of nasopharyngeal colonization when mice were challenged with a heterologous strain of nontypeable H. influenzae. These results suggest that intranasal immunization with Hap formulated with CT- **E29H** may be a valuable vaccine strategy for the prevention of nontypeable H. influenzae disease.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: *Bacterial Outer Membrane Proteins--immunology--IM; *Haemophilus Infections--immunology--IM; *Haemophilus Infections --prevention and control--PC; *Haemophilus influenzae--immunology--IM; *Nasopharynx--immunology--IM; *Nasopharynx--microbiology--MI; Adjuvants, Immunologic--administration and dosage--AD; Administration, Intranasal; Antibodies, Bacterial--immunology--IM; Bacterial Adhesion--immunology--IM; Bacterial Outer Membrane Proteins--administration and dosage--AD; Bacterial Outer Membrane Proteins--genetics--GE; Blotting, Western; Cell Line; Cloning, Molecular; Enzyme-Linked Immunosorbent Assay; Epithelial Cells--immunology--IM; Immunity, Mucosal--immunology--IM; Immunization; Immunoglobulin A--immunology--IM; Immunoglobulin G--immunology--IM; Mice; Mice, Inbred BALB C

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Antibodies, Bacterial); 0 (Bacterial Outer Membrane Proteins); 0 (Hap protein); 0 (Immunoglobulin A); 0 (Immunoglobulin G)

Record Date Created: 20020930

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E18        2  GLU285LYS
E19       71  GLU286
E20        7  GLU286ASP
E21        7  GLU286CYS
E22        1  GLU286TYR288
E23       22  GLU287
E24        7  GLU287MET

          Enter P or PAGE for more
?p

Ref    Items  Index-term
E25       19  GLU288
E26        1  GLU288ALA
E27       12  GLU289
E28        1  GLU289FWDARWLYS
E29       45  GLU29
E30       36  GLU290
E31        6  GLU2904GLY
E32        6  GLU291
E33        4  GLU291LYS
E34       25  GLU292
E35        7  GLU293
E36        2  GLU294

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Set      Items   Description
S1          13   E1-E6
S2          11   'GLU29'
S3          45   'GLU29'
S4           0   S3 AND CHOLERA?
S5         160   GLU (2N) 29
S6           8   S5 AND CHOLERA?
S7           4   'GLU25ASP'
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 7/8/1     (Item 1 from file: 155)
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14465467   22477042   PMID: 12589569
  Engineering new metal specificity in EF-hand peptides.
11 20 2002


 7/8/2     (Item 1 from file: 34)
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11430924   Genuine Article#: 652DU   Number of References: 31
Title: Engineering new metal specificity in EF-hand peptides  (ABSTRACT
    AVAILABLE)
Publication date: 20030200
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; CHEMISTRY,
    INORGANIC & NUCLEAR
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Descriptors--Author Keywords: calmodulin ; EF-hands ; metal chelation ;
fluorescence ; biosensors
Identifiers--KeyWord Plus(R): CALCIUM-BINDING MOTIF; CALMODULIN; PROTEIN;
LUMINESCENCE; SELECTIVITY; CONSTANTS; TOXICITY; AFFINITY; NUMBER; CELLS

7/8/3 (Item 1 from file: 73)
11974088 EMBASE No: 2003084806
Engineering new metal specificity in EF-hand peptides
2003

7/8/4 (Item 1 from file: 172)
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02886768 EMBASE No: 2003084806
Engineering new metal specificity in EF-hand peptides
2003
AUTHOR KEYWORDS: Calmodulin; EF-hands; Metal chelation; Fluorescence;
Biosensors
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08248393 94314415 PMID: 8039872

Construction and characterization of recombinant Vibrio cholerae strains producing inactive cholera toxin analogs.

Hase C C; Thai L S; Boesman-Finkelstein M; Mar V L; Burnette W N; Kaslow H R; Stevens L A; Moss J; Finkelstein R A

Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri, Columbia 65212.

Infection and immunity (UNITED STATES) Aug 1994, 62 (8) p3051-7, ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI17312; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The catalytic A subunit of cholera toxin (CT-A) is capable of ADP-ribosylating the guanine nucleotide-binding protein, which regulates cell adenylyl cyclase, leading to the life-threatening diarrhea of cholera. Amino acids involved in the enzymatic activity of CT-A have previously been identified. By means of site-directed mutagenesis, an analog of the CT-A subunit gene was created with codon **substitutions** for both Arg-7 and Glu-112, each of which has been shown to produce **subunits** lacking ADP-ribosyltransferase activity. The mutated gene fragment was exchanged for the wild-type copy in the previously cloned ctxAB operon from El Tor biotype, Ogawa serotype **Vibrio** cholerae strain 3083, which produces CT-2. Further, the zonula occludens toxin gene, zot, was inactivated by an insertional **mutation** to create the new plasmid construct pCT-2*. Additionally, a DNA fragment encoding the B **subunit** of CT-1 (CT produced by classical biotype, Inaba serotype V. cholerae strain 569B) was exchanged for the homologous part in pCT-2*, resulting in the creation of pCT-1*. These plasmid constructs were introduced into the CT-negative V. cholerae **mutant** strain JBK70 (E1 Tor biotype, Inaba serotype); CT-A-B+ derivatives CVD101 and CVD103 of classical biotype Ogawa and Inaba serotype strains 395 and 569B, respectively; El Tor biotype Inaba and Ogawa serotype strains C6706 and C7258, respectively, recently isolated in Peru; and O139 (synonym Bengal) strain SG25-1 from the current epidemic in India. Recombinant toxins (CT-1* and CT-2*), partially purified from culture supernatants of transformed JBK70, were shown to be inactive on mouse Y1 adrenal tumor cells and in an in vitro ADP-ribosyltransferase assay. CT-1* and CT-2* reacted with polyclonal and monoclonal antibodies against both A and B **subunits** of CT. The toxin analogs reacted with antibodies against CT-A and CT-B on cellulose acetate strips and in a GM1 enzyme-linked immunosorbent assay; they reacted appropriately with B- **subunit** epitype-specific monoclonal antibodies in checkerboard immunoblots, and they formed precipitin bands with GM1-ganglioside in Ouchterlony tests. However, the reactions of the **modified** proteins with anti-A- **subunit** monoclonal antibodies were weaker than the reactions with wild-type holotoxins. V, cholerae strains carrying ctxA*, with either ctxB-1 or ctxB-2, and inactivated zot genes were created by homologous recombination. The recombinant strains and the purified toxin analogs were inactive in the infant rabbit animal model.(ABSTRACT TRUNCATED AT 400 WORDS)

Tags: Animal; Support, U.S. Gov't, P.H.S.

Descriptors: *Cholera Toxin--biosynthesis--BI; *Cholera Vaccines --biosynthesis--BI; *Vaccines, Synthetic--biosynthesis--BI; *Vibrio cholerae--genetics--GE; Base Sequence; Cholera Toxin--genetics--GE; Cholera Toxin--toxicity--TO; Genes, Bacterial; Molecular Sequence Data; Plasmids; Rabbits

CAS Registry No.: 0 (Cholera Vaccines); 0 (Plasmids); 0 (Vaccines, Synthetic); 9012-63-9 (Cholera Toxin)

Record Date Created: 19940824

Record Date Completed: 19940824

08597972 95286289 PMID: 7768621

Construction of nontoxic derivatives of cholera toxin and characterization of the immunological response against the A subunit.

Fontana M R; Manetti R; Giannelli V; Magagnoli C; Marchini A; Olivieri R; Domenighini M; Rappuoli R; Pizza M

IRIS, Biocine Immunobiological Research Institute Siena, Italy.

Infection and immunity (UNITED STATES) Jun 1995, 63 (6) p2356-60, ISSN 0019-9567 Journal Code: 0246127

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Using computer modelling, we have identified some of the residues of the A subunit of cholera toxin (CT) and heat-labile toxin that are involved in NAD binding, catalysis, and toxicity. Here we describe the site-directed mutagenesis of the CT gene and the construction of CT mutants. Nine **mutations** of the A **subunit** gene were generated. Six of them encoded proteins that were fully assembled in the AB5 structure and were nontoxic; these proteins were CT-D53 (Val-53-->Asp), CT-K63 (Ser-63-->Lys), CT-K97 (Val-97-->Lys), CT-K104 (Tyr-104-->Lys), CT-S106 (Pro-106-->Ser), and the double **mutant** CT-D53/K63 (Val-53-->Asp, Ser-63-->Lys). Two of the **mutations** encoded proteins that were assembled into the AB5 structure but were still toxic; these proteins were CT-H54 (Arg-54-->His) and CT-N107 (His-107-->Asn). Finally, one of the **mutant** proteins, CT-E114 (Ser-114-->Glu), was unable to assemble the A and the B **subunits** and produced only the B oligomer. The six nontoxic **mutants** were purified from the culture supernatants of recombinant **Vibrio** cholerae strains and further characterized. The CT-K63 **mutant** , which was the most efficient in assembly of the AB5 structure, was used to immunize rabbits and was shown to be able to induce neutralizing antibodies against both the A and B **subunits** . This molecule may be useful for the construction of improved vaccines against cholera.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: *Cholera Toxin--immunology--IM; Base Sequence; Cholera Vaccines--immunology--IM; Immunization; Molecular Sequence Data; Mutation; Rabbits; Structure-Activity Relationship

CAS Registry No.: 0 (Cholera Vaccines); 9012-63-9 (Cholera Toxin)

Record Date Created: 19950705

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